## REMARKS

Claims 10-13, 18 and 23-39 are pending in the present application. By virtue of this response, claims 23 and 35 have been amended. Accordingly, claims 10-13, 18 and 23-39 are currently under consideration. Amendment of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented. No new matter has been added.

### *Supplemental Application Data Sheet*

Submitted herewith is a Supplemental Application Data Sheet to correct a typographical error in the title of the application.

### *Supplemental Information Disclosure Statement*

A Supplemental Information Disclosure Statement accompanies this response and Applicants respectfully request consideration of the listed references.

### *Priority*

The Examiner states that claims of the present application are only entitled to priority of the filing date of the parent application 10/814,634, filed 4/1/2004.

Applicants submit that such priority information is indicated in the Supplemental Application Data Sheet filed on July 26, 2010 as well as the Supplemental Data Sheet submitted herewith.

### *Specification*

The disclosure is objected to because of the following informalities. The Examiner states that in the brief description of the drawings on page 7 of the instant application, there is a reference to a 30 bp fragment in figure 2; however, the fragment in figure 2 appears to be 40 bp, not 30 bp.

Figure 2 of the instant application shows a 37 bp fragment. Accordingly, the brief description of the drawings on page 7 has been amended to recite "Figure 2 shows the 37 bp fragment."

A similar amendment has been made to the first paragraph of Example 1 to recite "[A] 37bp fragment (containing three tandem AUUUA motifs and flanking IL-1.beta. 3'UTR sequence) obtained by annealing two complementary synthetic oligonucleotides (see FIG. 2) was subcloned."

In view of this amendment, Applicants respectfully request withdrawal of this objection.

***Claim Rejections – 35 USC § 103(a)***

Claims 10-13 and 23-39 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Zubiaga et al. ("Zubiaga", Molecular Cell Biology, 1995, Vol. 15, No. 4, pages 2219-2230; of record in the IDS), in view of Banholzer et al. ("Banholzer", Molecular Cellular Biology, 1997, Vol. 17, No. 6, pages 3254-3260; of record in the IDS), in view of Lemm and Ross (Molecular and Cellular Biology, 2002, Vol. 22, No. 12, pages 3959-3969; of record in the IDS). Applicants respectfully traverse this rejection.

Applicants submit that Zubiaga, Banholzer and/or Lemm and Ross alone or in combination, do not render claim 10 and its dependent claims obvious. Claim 10 and its dependent claims are directed to methods of screening using a DNA expression system, wherein the mRNA which is transcribed from said expression system comprises at least one copy of a heterologous mRNA instability sequence comprising one or more coding region determinant (CRD) or fragment thereof.

Zubiaga et al. focuses on identifying the minimal AU-rich motif capable of destabilizing mRNA. Various constructs comprising different ARE sequences inserted into the 3'UTR of the β-globin gene were made and transiently transfected into NIH 3T3 cells. The stability of mRNA containing different sequences were evaluated and compared based on Northern blot analyses. As

acknowledged by the Examiner, Zubiaga neither teaches an assay system for screening compounds which destabilize mRNA, nor teaches a coding region instability determinant as the instability sequence.

Banholzer et al. focuses on understanding the mechanisms by which rapamycin ("RAPA"), a known immunosuppressive drug, downregulates IL-3 mRNA in a tumor mast cell line. Genomic IL-3 wild-type sequences or a sequence lacking the AU-rich element (ARE) were transfected into separate tumor cell lines. The effects of rapamycin on the IL-3 mRNAs were evaluated. To determine whether the 3'UTR of IL-3 would confer sensitivity to a heterologous transcript, Banholzer et al. also examined the effect of rapamycin on AP reporter constructs carrying the 3'UTR of IL-3 with or without deletion of the ARE.

Furthermore, Banholzer concluded that "IL-3 3'UTR could confer RAPA sensitivity to reporter transcripts, provided that the 3'UTR sequence was intact." Banholzer thus conveys to a person of ordinary skill in the art that, for the purpose of studying the effect of rapamycin on IL-3 mRNA, it is important to keep the mRNA instability sequence in its natural state. As acknowledged by the Examiner, Banholzer does not teach a coding region instability determinant as the instability sequence.

The Examiner relies on Lemm and Ross as allegedly teaching that a 249 nucleotide coding region from c-myc destabilizes c-myc and that such sequence destabilizes β-globin mRNA when inserted in frame within the coding region of β-globin. The Examiner thus concludes that "it would have been obvious to one of ordinary skill in the art to use the cell lines with constructs that have instability sequence as taught by either Zubiaga et al. or Banholzer et al. to test compounds that affect coding region instability determinants (CDR) from c-myc." Page 9 of Office Action. Applicants respectfully disagree.

As discussed in Lemm and Ross, the coding region instability determinant (CRD) functions independently of the AU-rich element to make the mRNA instable. Page 3959, right

column, second paragraph. Lemm and Ross teach that the CRD "must be translated to destabilize the mRNA," and that "[p]lacing a translational stop codon upstream of the CRD stabilizes the chimeric RNA." Page 3959, right column, second paragraph. Lemm and Ross further discuss regulation of c-myc mRNA decay by "translational pausing" in the CRD. One of ordinary skill in the art reading Lemm and Ross would clearly understand that the CRD discussed therein has to be present in the coding region in order for "translational pausing" to occur, and that placing the CRD into the 3'UTR would be ineffective in destabilizing mRNA. This is also acknowledged by the Examiner, who states that the 249 nucleotide coding region from c-myc "destabilizes beta-globin mRNA when inserted in frame within the coding region of said beta-globin gene." Page 9 of Office Action.

Accordingly, Applicants respectfully submit that Lemm and Ross not only provide no motivation but also teach away from inserting a CRD into an heterologous 3'UTR construct of Zubiaga, which is designed to identify the minimal AU rich sequence motif that destabilizes mRNA or from inserting a CRD into the 3'UTR of IL-3 in a construct disclosed by Banholzer which is designed to test the effect of rapamycin on the 3'UTR of β-globin.

Accordingly, Applicants respectfully submit that Zubiaga et al. and Banholzer et al. either alone or in combination with Lemm and Ross do not render claim 10 and its dependent claims obvious. In view of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

***Claim Rejections – 35 USC § 112, 2nd paragraph***

Claims 23-25 and 35-36 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention.

Solely in an effort to expedite prosecution, claim 23, from which claims 24-25 depend, and claim 35, from which claim 36 depends, have been amended to delete the word "derived." The

rejection is thus rendered moot in view of the claim amendments. Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §112.

## CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 608352000101. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: June 24, 2011

Respectfully submitted,

Electronic signature: /Eva Hannak/
Eva Hannak
Registration No.: 64,063
MORRISON & FOERSTER LLP
755 Page Mill Road
Palo Alto, California 94304-1018
(650) 813-5726